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Surgical Management of Epilepsy

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Therapy with anticonvulsant drugs reduces the frequency and severity of seizures in many but not all epileptic patients. Unfortunately, in a significant number control remains poor even when maximal doses of multiple anticonvulsant drugs are given. Some of these patients are candidates for surgical treatment of epilepsy. The operative management of convulsive disorders is a well-established technique and is available in some centers. In selected cases, such operations are both safe and effective, with good long-term improvement or complete control in 76 percent of patients. We have summarized the 24-year experience with surgical operation for epilepsy at the University of Washington Medical Center.

MANAGEMENT OF CONVULSIVE DISORDERS continues to be a vexing problem even with the introduction of effective anticonvulsant drugs. A reasonable figure for the prevalence of epilepsy (when prevalence is based on two or more afebrile seizures) is about five to seven per 1,000.[1,2] It is widely reported anecdotally that most of these cases are controlled on medication. Seizure control, however, is a subjective judgment and its definition is dependent on many variables which include patient reporting and physician interpretation. Reynolds has critically reviewed several published series concerned with the adequacy of seizure control in patients receiving anticonvulsant drugs; these data indicate that in only 30 to 37 percent of all types of seizure disorders are patients seizure free because of medication over a two-year follow-up period.[1] At the end of ten years only 10 percent of all patients had remained seizure-free. There are subpopulations that do significantly better, and an occasional seizure may be tolerable for certain patients, but careful epidemiologic studies do not support the contention that seizures in most epileptic patients are completely controlled by medications. Furthermore, chronic anticonvulsant medications are not without serious side effects. The problems of Purkinje cell loss and cerebellar ataxia, abnormal folate metabolism, hematologic toxicity, sedation, psychotic reactions, abnormalities of connective tissue, endocrine effects and so-called allergic hypersensitivity have all been reviewed in detail.[3] Furthermore, in approximately 20 to 30 percent of epileptic patients, seizures are uncontrolled by any standard with current anticonvulsant medications, even with careful monitoring of serum drug levels. In patients with seizures of focal origin, particularly temporal lobe foci, control is espe-

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cially difficult to achieve. In some patients in whom seizures are not fully controlled by anticonvulsant medications, surgical operation is a treatment option. Robb has conservatively estimated that 10 percent of all patients with seizures, or roughly 105,000 people in the Unitel States, may be candidates for epilepsy operations.[2]

Epilepsy has been surgically treated since the first Stone Age trephinations. The long and often colorful history of operations for seizure control includes blood-letting, fenestration of the dura, cervical sympathectomy, muscle-to-brain grafts, adrenalectomy, clitoridectomy and bowel resection; these have been reviewed by Marshall.[4] The modern era for both the medical and surgical treatment of the epilepsies began in the mid-19th century with the work of Fritsch and Hitzig, Hughlings Jackson, Gowers and later Horsley. These pioneers in the study of the central nervous system described not only the various clinical presentations of seizures, but also cortical stimulation and localization experiments which began to focus on abnormal neuronal mechanisms as causing epilepsy. With this background, Horsley and then Foerster first described subpial cortical resections for the control of seizures. Following the advent of modern electroencephalography and anesthesia, Penfield and his students developed the modern techniques for epilepsy operations. This paper discusses the rationale for this procedure, methods of patient selection, and the long-term results of surgical therapy for epilepsy at the University of Washington Medical Center over the past 24 years.

Patient Selection

The criteria for selection of patients as operative candidates have been made standard. Such patients must have intractable seizures which are refractory to adequate medical therapy; the epileptic focus generating the seizures must be identified; this focus must be in dispensible cortex. The first criterion is the most important and a thorough attempt must be made to control the seizures with anticonvulsant drugs. A trial of standard doses of diphenylhydantoin (Dilantin®) alone is insufficient. The focus is localized initially by obtaining a careful description of a typical seizure. These data should be confirmed by detailed electroencephalographic (EEG) localization. Findings on contrast studies (usually angiography and pneumoencephalography) should be consistent with the final formulation of the problem. Finally, this focus must be located in a part of the cortex which can be surgically removed without significant neurological deficit. Therefore, a patient is not a candidate for surgical therapy if the focus is located in primary speech cortex.

For patients in whom medical therapy has failed, evaluation begins with routine history (and family history), examination, detailed description and preferably observation of a typical attack, as well as basic EEG studies including sleep tracings. Next the patient is admitted to hospital for more detailed diagnostic studies. These commonly include pneumoencephalography, computerized axial tomography, special localizing EEG studies and neuropsychological testing. Angiography including lateralization of speech by the Wada test (intraarterial ultra-short-acting barbiturate) may also be done. If an obvious structural lesion can be found (neoplasm, arteriovenous malformation [AVM]), the appropriate operation can be undertaken. If the seizure focus can be discretely localized to one area on one side of the brain in nonessential cortex the patient should be considered for surgical treatment.

This approach to the treatment of focal epilepsy is based on current theoretical models of epileptogenic neurons as reviewed by Ward.[5] The concept is fundamentally simple: to remove that aggregate of abnormal neurons that are responsible for the ictus while sparing vital parts of the brain. A number of observations suggest that effective resections depend on other variables also. For example, temporal lobe resection is more likely to result in long-term benefit when the medial temporal structures (especially hippocampus) are included. On the other hand, success does not seem to depend on removal of insular cortex even if found to be abnormal on direct recording. The collected results of epilepsy operations in highly selected populations of medically intractable disorders are uniformly good in many reported series, with approximately 75 percent of patients seizure free or significantly improved postoperatively.[6,9,10]

University of Washington Series

The data presented here are based on a review of the records of 45 patients (47 operations) treated by three surgeons between 1952 and 1976. There have been no operative deaths; in one patient a craniotomy was done but no abnormal focus was noted at the time of electro-

TABLE 1.—*Age in Years at the Time of Seizure Onset and at the Time of Epilepsy Operation*

	Age (Operation)	Age (Onset)
Mean in years	26.6	12.1
Range in years	7-47	1-43
Number of cases by decades		
0-9	0	21
10-19	10	15
20-29	23	6
30-39	11	1
40-49	4	1

TABLE 2.—*Type of Seizures*

	Primary	Secondary
Major motor	9	18
Complex partial	25	2
Focal	7	2
Secondarily generalized	0	5
Absence	1	3
Akinetic	1	1
Other	2	3

TABLE 3.—*Resection Site*

	Left	Right	Total
Frontal	1	8	9
Temporal	14	17	31
Partial	1	2	3
Hemispherectomy	1	0	1
Temporoparietal	0	1	1
Frontoparietal	1	0	1
No resection	1	0	1

corticography and therefore no tissue was resected. The age of onset of seizures in this population is shown in Table 1. In 81 percent of our patients, seizures began before the age of 20; this figure is in close agreement with those in other large series.[7,8] The age distribution at the time of operation is also shown in Table 1 and likewise corresponds with published data.[8] The duration of our follow-up on these 45 patients averages 4.4 years and ranges between ten weeks and 20 years.

Complex partial seizures (also called temporal lobe or psychomotor epilepsy) constituted the majority of the types of attacks in our series (Table 2). Major motor (grand mal) and focal motor or sensory seizures were the next most common. Major motor and secondarily generalized seizures were the most common secondary types of attacks. As shown in Table 3, the temporal lobe was the most common resection site.

Our results over 24 years are very similar to those reported in the other major series with similar selection criteria.[6,9,10] As shown in Table 4, 36 percent of all patients were seizure-free for

TABLE 4.—*Results*

	Seizure Free	Improved	Unchanged	Total	Percent
Frontal	2	5	2	9	15
Temporal	13	13	4	30	64
Parietal	0	0	2	2	
Hemispherectomy	1	0	0	1	
Temporoparietal	0	1	0	1	21
Frontoparietal	1	0	2	3	
No resection	0	0	1	1	
Total	17	19	11	47	
Percent	36	40	24		
	76				

the period of follow-up (excluding the immediate postoperative period); an additional 40 percent were improved. Improvement is defined as a reduction in the seizure frequency of such a magnitude that there was a major beneficial impact on the patient's life. In practice, this usually implied a decrease in seizure frequency of 50 percent or more; often only occasional seizures were reported. Therefore, 76 percent of patients were seizure-free or significantly improved, while 24 percent (11 patients) showed no improvement. These figures are in close agreement with those reported by Rasmussen in 1974 based on 629 cases.[10]

In 36 percent of our patients in whom temporal lobe resection was done, there also was a psychiatric diagnosis. Those patients with complex partial seizures and no psychiatric diagnosis had a good result in 95 percent of cases compared with a good result in 70 percent of cases when psychiatric problems were diagnosed. The problem of complex partial seizures concomitant with psychiatric disturbance is, of course, one of the major variables which complicate interpretation of this kind of data. Of the two patients operated upon twice, one improved following the second procedure; both had psychiatric diagnoses as did the patient in whom craniotomy was done but no resection. The latter was unchanged postoperatively.

The light microscopic pathological findings in 36 cases of tissue removed at epilepsy operation are summarized in Table 5. Gliosis of both cortex and deep nuclei predominated, followed by neuronal loss and satellitosis—all nonspecific changes. Four tumors were reported. Some of the epileptic tissue has also been examined biochemically and a decrease in sodium, potassium

TABLE 5.—*Pathology (n=36)*

	Temporal	Frontal	Parietal	Hemispherectomy	Total
Gliosis (white)	12	3	..	..	15
Gliosis (grey)	5	1	1	..	7
Gliosis (deep)	9	..	..	..	9
Neuronal loss (grey)	4	2	..	..	6
Neuronal loss (deep)	5	..	..	..	5
Satellitosis	3	1	1	..	5
Edema	1	..	..	..	1
Atrophy	2	..	..	..	2
Cicatrix	2	..	..	..	2
Calcification	2	2	..	..	4
Necrosis	1	..	..	1	2
Neuronal pyknosis	3	..	..	..	3
Cystic	4	1	..	..	5
Hemosiderin	4	1	..	..	5
Glioma, grade 1	1	..	..	..	1
Oligodendroglioma	..	2	..	..	2
Meningioma	..	1	..	..	1
AVM	1	..	..	..	1
Angioma	1	..	1	..	2
Status marmoratus	..	..	1	..	1
No diagnostic alteration	5	2	..	..	7

AVM = arteriovenous malformation

TABLE 6.—*Probable Etiological Events*

Head injury	11
Porencephaly	2
Encephalitis	2
Abscess	1
Dermoid	2
Tumor	4
AVM/Angioma	3
Perinatal disease	6

AVM = arteriovenous malformation

adenosinetriphosphatase (ATPase) activity has been recently reported.[11] This enzyme system is felt to be at least in part responsible for maintaining the ionic gradient across bioactive membranes. A summary of more probable gross causes in 31 of the 45 cases is shown in Table 6.

Discussion

Modern surgical resection for the treatment of medically intractable epilepsy is a somewhat neglected but valuable adjunctive form of therapy. The goals and risks of this procedure in a highly selected population are well documented.[6,10] Patients are candidates (1) in whom adequate control is not achieved with anticonvulsant drugs or who, because of toxicity or idiosyncratic reaction, are unable to take the appropriate medication and (2) in whom there is a localizable lesion in nonessential cortex. Other considerations are the presence of additional neurologic disability such as mental retardation or psychiatric illness. While fixed deficits such as retardation will not be improved, there is evidence that seizure control may alter some behavioral abnormalities. It is an especially common observation that patients with temporal lobe seizures are behaviorally improved postoperatively.[6,13] A final important consideration is the patient's motivation and ability to tolerate the rigors of both the evaluation for surgical operation and craniotomy under local anesthesia.

Because corticographic localization of electrical abnormality is essential to maximize the beneficial results of surgical therapy for epilepsy, general anesthesia is seldom used. This, of course, does not apply in children. The operation is usually done with some sedation and local anesthetic. This arrangement is, obviously, a major stress for the patient. Our experience has been that the motivation for cure or improvement is great enough that the procedures are tolerable for the patients we select.

Since local anesthetic is used, the risk of general anesthesia is obviated. The remaining unlikely risks are intraoperative catastrophe (such as vascular occlusion) or postoperative complications such as wound infection, pulmonary embolus or pneumonia. The final risk is that the procedure will fail to improve seizure control.

Our results are similar to most other series in reporting a success rate of approximately 75 percent when success is defined as no or fewer seizures when medication is given.[6,9,10] Our practice has been to maintain the preoperative medications for at least one year following the procedure. If at that time no seizures have occurred the drugs may be stopped. Under this protocol, 36 percent of the patients in this series are seizure free and an additional 40 percent are significantly improved. These figures are so encouraging that it is surprising that more operations for intractable seizures are not done.

The University of Washington is one of the few centers routinely carrying out surgical operations for epilepsy, yet only 50 epileptic patients have been operated upon in 24 years. Why should this be the case? Several reasons may be listed: (1) ignorance of the operation's availability, (2) expense, (3) patient fear, (4) reluctance of primary doctors to suggest an operation when many

anticonvulsants are available. We believe that surgical treatment can make a major beneficial impact on the lives of properly selected patients; the complication rate is low and the results usually good or excellent.

Because of the suggested relationship between seizures and behavioral disorders, consideration should also be given to the timing of epilepsy operations. The lives of patients with intractable seizures are profoundly influenced not only by the ictal events, but also by the continual threat of seizures. Moreover, even in the absence of specific intellectual deficits, a child with continually abnormal electrical activity may be retarded in learning simply on the basis of time available to learn. They may also be retarded in their social interactions both in school and at home. Behavioral disturbances and dependence are common concomitants of intractable epilepsy. For these reasons, early consideration should be given to surgical operation when aggressive medical management has failed. Table 1 shows that the mean age at operation in our series was delayed 14.5 years beyond the mean age of seizure onset. The final results in terms of both seizure control and improved interpersonal relationships may be favorably influenced by early surgical intervention.

Finally, it should be noted that a variety of surgical techniques other than cortical resection have been proposed. Some of these, including stereotaxic lesions in several deep targets, are encouraging. The most promising are radiofrequency lesions in the medial temporal lobe including amygdala, hippocampus and fornix.[12] More recently cerebellar stimulation has been advocated, but the possible benefits of this technique remain both theoretically and practically conjectural.

Summary

The theoretical basis and history of surgical treatment of epilepsy have been briefly reviewed. The limits of medical management of seizures are discussed, and criteria for patient selection as surgical candidates are summarized. While operations for epilepsy are done infrequently at most centers, those neurosurgical units with a major commitment in this area do a significant number of such operations. The process of patient selection includes multiple EEG's, angiography, speech localization, pneumoencephalography or computed tomography (CT) scanning and neuropsychological testing. Those patients with focal seizure disorders which do not involve vital structures (such as primary speech cortex) should be considered for epilepsy surgery.

The data presented are based on a review of the records of 45 patients in whom a total of 47 operations were done in the past 24 years; there were no deaths. Of these patients, 76 percent are seizure-free or improved for the follow-up period, which averages 4.4 years. Pathological findings in resected tissue are nonspecific in most cases. However, four brain tumors, two angiomas and one AVM were included in the series.

Finally, those patients with focal seizures in whom medical management fails or in whom complications of drug therapy develop might be given earlier consideration as surgical candidates.

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